

**AMENDMENTS****In the Claims:**

Claim 1. (Currently Amended) Isolated photoprotein containing an amino acid sequence which:

- a) is able to bind coelenterazine and calcium, producing bioluminescence;
- b) is identical by at least 90% to SEQ ID NO: 1 (Clytin);
- c) is in sequence alignment with SEQ ID NO: 1 (Clytin), ~~presents~~ and comprises one of the following single or multiple substitutions (the residue positions are referred with reference to SEQ ID NO: 1):
  - i) C<sub>54</sub>→S;
  - ii) S<sub>132</sub>→C;
  - iii) K<sub>48</sub>→R, N<sub>195</sub>→D;
  - iv) Q<sub>68</sub>→R, A<sub>90</sub>→V, T<sub>184</sub>→I;
  - v) Y<sub>82</sub>→F, K<sub>110</sub>→N, F<sub>125</sub>→L, S<sub>149</sub>→R;
  - vi) G<sub>142</sub>→C;
  - vii) I<sub>53</sub>→V, S<sub>149</sub>→R;
  - viii) N<sub>18</sub>→D, I<sub>40</sub>→V, K<sub>56</sub>→R;
  - ix) Gly<sub>58</sub>→Glu, Asp<sub>69</sub>→Val, Ala<sub>70</sub>→Cys, Lys<sub>76</sub>→Arg, Lys<sub>77</sub>→Gly, Ile<sub>78</sub>→Cys, Asp<sub>81</sub>→Glu, Val<sub>86</sub>→Ile, Glu<sub>87</sub>→Ala, Ala<sub>90</sub>→Gln, Val<sub>92</sub>→Leu, and Glu<sub>97</sub>→Gln

or a functional derivative or fragment thereof.

Claim 2. (Original) The photoprotein of claim 1, containing an amino acid sequence identical by at least 95% to SEQ ID NO: 1.

Claim 3. (Original) The photoprotein of claim 2, containing an amino acid sequence identical by at least 98% to SEQ ID NO: 1.

Claim 4. (Original) The photoprotein of claim 3, containing an amino acid sequence which is selected from the group consisting of SEQ ID NO: 2, 3, 4, 5, 6, 7, 8, 9, 10.

Claim 5. (Previously Presented) A photoprotein according to claim 1, wherein said amino acid sequence is fused to a mitochondrial target sequence.

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Claim 6. (Withdrawn) An isolated polynucleotide encoding a photoprotein according to claim 1.

Claim 7. (Withdrawn) The polynucleotide of claim 6, having the sequence of SEQ ID NO: 11, 12, 13, 14, 15, 16, 17, 18, 19.

Claim 8. (Withdrawn) An expression vector containing a polynucleotide according to claim 6.

Claim 9. (Withdrawn) A prokaryotic or eukaryotic host cell containing the vector of claim 8.

Claim 10. (Withdrawn) A mammalian host cell according to claim 9.

Claim 11. (Withdrawn) A method in vitro for detecting changes in intracellular calcium concentration which comprises:

- a) providing a cell expressing a photoprotein according to claim 1;
- b) contacting the cell with an agent stimulating calcium influx or calcium release from intracellular stores;
- c) detecting the photoprotein bioluminescence.

Claim 12. (Withdrawn) A method of screening compounds modulating intracellular calcium concentration, which comprises:

- a) providing a cell expressing a photoprotein of claim 1;
- b) contacting the cell with the candidate compound;
- c) detecting the bioluminescence of the photoprotein.

Claim 13. (Withdrawn) A method according to claim 11, which is carried out in a high-throughput format.

Claim 14. (Withdrawn) A method according to claim 13, which is carried out with a high throughput optical screening apparatus suited for multi-sample analysis.

Claim 15. (Withdrawn) The use of a photoprotein according to claim 1 as intracellular calcium indicator.

Claim 16. (Withdrawn) The use of a photoprotein according to claim 15 in a cell-based high throughput assay.

Claim 17. (Withdrawn) The use of a photoprotein according to claim 1 for the preparation of a diagnostic composition.